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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,406	01/09/2002	John B. Sheehan	1011U-1	9034

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EXAMINER	
MAHATAN, CHANNING	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/042,406

Applicant(s)

SHEEHAN ET AL.

Examiner

Channing S. Mahatan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-32 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 Sheets.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

ART UNIT DESIGNATION

The Art Unit designated for this application has changed. Applicants are hereby informed that future correspondence regarding this application should be directed to Group Art Unit 1631.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 1-32.

Claims Rejected Under 35 U.S.C. 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 22-31 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

NON-STATUTORY SUBJECT MATTER

Claims 22-31 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claimed invention is directed to a "computer program for designing primer pairs for amplifying a target nucleic acid sequence" (i.e. computer code).

M.P.E.P. section 2106 1(a) states:

Similarly, computer programs claimed as computer listings per se, i.e., the descriptions or expressions of the programs, are not physical ****>"things."** They are neither computer components nor< statutory processes, as they are "acts" being performed. Such claimed computer programs do not define any structural and functional interrelationships between the computer program and other claimed ****>elements of a computer<** which permit the computer program's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a computer program **>** is a computer element which< defines structural and functional interrelationships between the computer program and the ***>rest of the computer<** which permit

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the computer program's functionality to be realized, and is thus statutory. Accordingly, it is important to distinguish claims that define descriptive material per se from claims that define statutory inventions.

The computer program of claims 22-31 fails to define any structural and functional relationship between the computer program and computer; therefore the claims do not recite statutory subject matter.

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 U.S.P.Q. 546 (B.P.A.I. 1986) and reiterated by the Court of Appeals in In re Wands, 8 U.S.P.Q. 2d 1400 at 1404 (C.A.F.C. 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

SCOPE OF ENABLEMENT

Claims 1-32 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the disclosed method for designing primer pairs for amplifying a target sequence wherein the step of evaluating a candidate primer set for the extent of coverage and overlap of said target sequence is by Dijkstra's algorithm (pages 4, 8, and 9) of

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the Specification), does not reasonably provide enablement for the step of evaluating a candidate primer set by any other means.

The specification depicts in Figure 1 a flow chart generally illustrating the primer selection process (page 4, lines 8-9). The primer selection process is described by performing a number of steps: 1) Selection of a sequence of interest (i.e. target or reference sequence) for amplification, wherein the sequence is downloaded into a sequence file (page 4, lines 9-11 and 26-31); 2) Removal (i.e. RepeatMasker) of repeat sequences (i.e. Alu and LINE) in the reference sequence (page 4, lines 14-15; and pages 4-5); 3) Analysis (i.e. Primer3, xprimer, PrimerSelect, Oligo) of non-repetitive (i.e. un-removed) sequences to establish a set of primer candidates that fit within at least two selection parameters (i.e. primer melting temperature, primer length, stringency of hybridization, existence of duplexes, specificity of hybridization, existence of a GC clamp, existence of hairpins, existence of sequence repeats, the dissociation minimum for a 3' dimer, the dissociation minimum for the 3' terminal stability range, the dissociation minimum for a minimum acceptable loop, percent maximum homology, percent consensus homology, the maximum number of acceptable sequence repeats, frequency threshold, or the maximum length of acceptable dimers and the like) (page 4, lines 15-21; and pages 5-7); and 4) Evaluation of the primer candidate set by an algorithm (i.e. Dijkstra's algorithm) to determine coverage and overlap of the reference/target sequence and selection of a subset of primers, wherein the chosen primer pairs allow one to amplify all the entire target sequence with reduced sequence amplification overlap and/or a minimal number of primer pairs. The specification (page 8-9) describes Dijkstra's algorithm which solves the single-source shortest-paths problem on a weighted, directed graph $G = (V, E)$ for the case in which all edge weights are non-negative.

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Dijkstra's algorithm maintains a set of vertices, S , whose final shortest-path weights from a source s have already been determined; all vertices v being elements of S , $d[v] = \delta(s, v)$. The algorithm repeatedly selects the vertex u as an element of $V-S$ with the minimum shortest-path estimate, inserts u into S , and relaxes all edges radiating from u . A priority queue Q that contains all the vertices in $V-S$, keyed by their d values, is maintained assuming that graph G is represented by adjacency lists. Thus, G in this case is the graph of linear coverage of the target sequence, Q is the queue of all vertices to be evaluated and S is the set of vertices selected. Once one set of vertices (pair of primer pairs) is selected that covers a particular area of the target sequence, the other vertices that include these pairs can be discarded. Further, specification describes the application of Dijkstra's algorithm evaluates the candidate primer pair by considering each primer pair as a "vertex" with an "edge", wherein an associated "cost" was assigned to each edge. The cost reflecting the amount of: a) the overlap of vertices (cost = the length of the overlap); b) the gap between two primer pairs (cost = $10 \times$ the length of the gap); and c) a fixed value for having to add another vertex to the set (which increased the number of primers that must be used). The lowest "cost" primer pairs are selected (total cost equals the sum of the costs of edges in the path).

Thus, the only disclosed algorithm to evaluate of a candidate primer set is "Dijkstra's algorithm". No other methods for designing primer pairs wherein the evaluation of a candidate primer set for the extent of coverage and overlap of said target sequence other than that based on Dijkstra's algorithm is taught. None appear to have been known in the art. No guidance, direction, or examples are provided such that one of ordinary skill in the art can practice the claimed invention.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

VAGUE AND INDEFINITE

Claim 1 and all claims dependent therefrom recite the phrase "having reduced overlap" which is vague and indefinite. It is unclear as to the metes and bounds "reduced overlap" is to encompass, however, applicants can resolve this issue by particularly pointing out the criteria/range that encompasses "reduced". Clarification of the metes and bounds, via clearer claim language, is requested.

Claims 1, 18, and 19 recite the phrases "target sequence" and "reference sequence" which is confusing. For example, claim 1 a "target sequence" in the preamble, however, the claimed steps recite, "reference sequence". The instant claim language fails to maintain consistent language terminology and therefore is found confusing. Clarification, via clearer claim language, is requested.

Claims 8, 10, 24, 25, and 27 contain the trademark/trade names (i.e. RepeatMasker, Oligo, xprimer, PrimerSelect, Primer3, and RepBase). Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. § 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade

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name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a computer program, computer system, or database and, accordingly, the identification/description is indefinite.

Claim 11 and all claims dependent therefrom recite the phrase "a minimal or substantially minimal number of primer pairs" which is vague and indefinite. It is unclear as to the metes and bounds "minimal or substantially minimal number" is to encompass, however, applicants can resolve this issue by particularly pointing out the criteria/range that encompasses "minimal" and "substantially minimal". Clarification of the metes and bounds, via clearer claim language, is requested.

OBJECTION TO DISCLOSURE

The disclosure is objected to because it contains an embedded hyperlinks and/or other forms of browser-executable code and delete them beginning on page 5, line 3; etc. Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See M.P.E.P. § 608.01 and § 608.01(p).

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INFORMATION DISCLOSURE STATEMENT

Several cited references on the information disclosure statement were lined through because of citation to website(s) pages, wherein the information on the said website(s) is continually update. Thus, information publicly available (i.e. date) cannot be confirmed.

Appropriate Correction Is Requested.

No Claims Are Allowed.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Channing S. Mahatan whose telephone number is (703) 308-2380. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina M. Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

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Date: *August 23 2003*

Examiner Initials: *CSM*

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800

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